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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/923,952 | 08/08/2001 | Mitsuyo Nagano | 212033US0 DIV | 2293 |

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| EXAMINER |
|---|
| GAMBEL, PHILLIP |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1644 | 7 |

DATE MAILED: 08/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) |
|---|---|---|
| | 09/923952 | NAGANO |
| | Examiner | Art Unit |
| | GAMBEL | 1644 |

*– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, ~~may a reply~~ be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☑ Responsive to communication(s) filed on 8/8/01

2a)☐ This action is **FINAL**. 2b)☑ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☑ Claim(s) _____ is/are pending in the application. 15-21

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☑ Claim(s) _____ is/are rejected. 15-21

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☑ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☑ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☑ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)). 08/836982

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☑ The translation of the foreign language provisional application has been received.

15)☑ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☑ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:



PAPER NO. 7

## DETAILED ACTION

1. Applicant's amendment, filed 8/8/01 (Paper No.27), has been entered.
Claim 1-14 have been canceled.
Claims 15-21 have been added.

Claims 15-21 are pending.

2. The following guidelines illustrate the preferred layout and content for patent applications. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

The following order or arrangement is preferred in framing the specification and, except for the reference to the drawings, each of the lettered items should appear in upper case, without underling or bold type, as section headings. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) Title of the Invention.
(b) Cross-Reference to Related Applications.
(c) Statement Regarding Federally Sponsored Research or Development.
(d) Reference to a "Sequence Listing," a table, or a computer program listing appendix submitted on compact disc (see 37 CFR 1.52(e)(5)).
(e) Background of the Invention.
    1. Field of the Invention.
    2. Description of the Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(f) Brief Summary of the Invention.
(g) Brief Description of the Several Views of the Drawing(s).
(h) Detailed Description of the Invention.
(i) Claim or Claims (commencing on a separate sheet).
(j) Abstract of the Disclosure (commencing on a separate sheet).
(k) Drawings.
(l) Sequence Listing, if on paper (see 37 CFR 1.821-1.825).

The instant specification does not appear to contain a Brief Summary of the Invention.

3. Applicant should amend the first line of the specification to update the status of the priority documents.

USSN 09/299,016 is now U.S. Patent No. 6,280,731.

4. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected.

Trademarks should be capitalized or accompanied by the ™ or ® symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

For example, "Dalbeco's" should be "Dulbeco's" on page 21, line 14 of the specification.

"BALB/c" is the proper designation of this mouse strain (See page 25, line 2 of the specification).

Appropriate corrections are required

5. Formal drawings submitted 8/8/01 comply with 37 CFR 1.84.

6 Claims 15-21: It is apparent that the AJvW-2 and AJvW-4 antibodies / hybridomas are required to practice the claimed invention. As required elements, they must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If they are not so obtainable or available, the enablement requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the pertinent hybridomas which produce these antibodies. See 37 CFR 1.801-1.809.

Given the disclosure (e.g. see column 15, paragraph 2) and the claims (e.g. see claims 3 and 16) encompassing the instant AJvW-2 and AJvW-4 antibodies / hybridomas designated FERM BP-5248 and 5250 set forth in U.S. Patent No. 5,916,805.; the conditions for the deposit of biological materials under 35 USC 112, first paragraph, with respect to AJvW-2 and AJvW-4 antibodies / hybridomas have been satisfied.

7. Claims 17 and 19 are objected to under 37 CFR 1.75 as being as substantial duplicates of claims 18 and 20, respectively. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claims 17-18 are drawn to the exact same antibody.
Similarly, claims 19-20 are drawn to the same exact antibody.

8. Claims 15-21 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claim 15 is indefinite in the recitation of "a variant of any of them" because the nature of the structural and/or functional properties of the "variant" is unclear and ambiguous. Further, the recitation of "any of them" lacks clear and unambiguous proper antecedent basis.

For examination purposes and given the broadest reasonable interpretation of the claims (see art rejections below) the recitation of "variant" reads on antibodies that von Willebrand factor.

B) Claims 15-21 are indefinite in the recitation of "when the monoclonal antibody is allowed to co-exist with a monoclonal antibody produced by a hybridoma which is selected from the group consisting of FERM BP--5248 (AJvW-2), FERM BP-5250 (AJvW-4) because the intent or meaning of this "limitation" is unclear and ambiguous.

For example, there is no reason to assume that one monoclonal antibody cannot exist with another monoclonal antibody. Further, the antecedent basis of the "monoclonal antibody" in the "limitation" is ambiguous, given the recitation of "monoclonal antibody" in the preamble of claim 15, 15 (a) and twice in 15 (b).

C) Applicant should specifically point out the support for any amendments made to the disclosure. See MPEP 714.02 and 2163.06

9 The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

11. For examination purposes and given the broadest reasonable interpretation of the claims, the recitation of "variant" reads on antibodies that von Willebrand factor.

For examination purposes and given the broadest reasonable interpretation of the claims, the recitation "when the monoclonal antibody is allowed to co-exist with a monoclonal antibody produced by a hybridoma which is selected from the group consisting of FERM BP--5248 (AJvW-2), FERM BP-5250 (AJvW-4) because the intent or meaning of this "limitation" reads on antibodies that von Willebrand factor.

12. Claims 15 and 16 are rejected under 35 U.S.C. § 102(b) as being anticipated by Benson et al. (U.S. Patent No. 5,202,264) (1449; AA) (see entire document).

Benson et al. teach von Willebrand factor-specific monoclonal antibodies, including antibodies that bind epitopes having a clinical significant in terms of bleeding tendency (e.g. see Detailed Description, including column 8, paragraph 5 and column 13, paragraphs 1-3). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced inhibitory von Willebrand factor-specific monoclonal antibodies.

13. Claims 15 and 16 are rejected under 35 U.S.C. § 102(b) as being anticipated by Fujimura et al. (Thromb. Haem. 68: 464-469, 1992)( (1449; AX) (see entire document).

Fujimura et al. teach von Willebrand factor-specific monoclonal antibodies, including antibodies that inhibit ristocetin-induced platelet aggregation and/or von Willebrand factor binding to GPIb (e.g., see Summary, Results and Discussion). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced inhibitory von Willebrand factor-specific monoclonal antibodies.

14. Claims 15 ,16 and 21 are rejected under 35 U.S.C. § 102(e) as being anticipated by Scarborough (U.S. Patent No. 5,744,584) (see entire document).

Scarborough teach von Willebrand factor-specific monoclonal antibodies, including antibodies that inhibit platelet adhesion to collagen, ristocetin-induced platelet aggregation and/or von Willebrand factor binding to GPIb (e.g., see Background Art, particularly column 2, paragraphs 2-3). Given the teachings of the anti-thrombotic properties of anti-von Willebrand factor antibodies (column 2, paragraph 3), the ordinary artisan would have immediately envisaged placing anti-von Willebrand factor monoclonal antibodies referenced in Scarborough in the pharmaceutical compositions, also taught by Scarborough (see Administration and Utility, on columns 7-8). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced inhibitory von Willebrand factor-specific monoclonal antibodies.

15. Claims 15, 16 and 21 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Scarborough (U.S. Patent No. 5,744,584) AND Scarborough (U.S. Patent No. 5,744,584)(1449; AA) AND Fujimura et al. (Thromb. Haem. 68: 464-469, 1992)( (1449; AX).

Scarborough teach von Willebrand factor-specific monoclonal antibodies, including antibodies that inhibit platelet adhesion to collagen, ristocetin-induced platelet aggregation and/or von Willebrand factor binding to GPIb (e.g., see Background Art, particularly column 2, paragraphs 2-3).

Benson et al. teach von Willebrand factor-specific monoclonal antibodies, including antibodies that bind epitopes having a clinical significant in terms of bleeding tendency (e.g. see Detailed Description, including column 8, paragraph 5 and column 13, paragraphs 1-3)

Fujimura et al. teach von Willebrand factor-specific monoclonal antibodies, including antibodies that inhibit ristocetin-induced platelet aggregation and/or von Willebrand factor binding to GPIb (e.g., see Summary, Results and Discussion).

Scarborough, Benson et al. and Fujimura et al. differ from the claimed invention by not explicitly teaching placing the inhibitory von Willebrand factor-specific antibodies in composition comprising a pharmaceutical acceptable carrier.

Given the teachings of the inhibitory properties of the referenced von Willebrand factor-specific antibodies taught by Scarborough, Benson et al. and Fujimura, including the anti-thrombotic properties of anti-von Willebrand factor antibodies (see column 2, paragraph 3 of Scarborough), the ordinary artisan would have been motivated to place the referenced inhibitory anti-von Willebrand factor monoclonal antibodies, including those referenced in Scarborough, in the pharmaceutical compositions, also taught by Scarborough (see Administration and Utility, on columns 7-8) to test the ability of such inhibit anti-von Willebrand factor antibodies to act as platelet adhesion or thrombus inhibitors.

It has been held by the Court that a compound and a carrier are obvious, if it is obvious in the art to utilize a carrier with related compounds. See In re Rosicky, 125 USPQ 341 (CCPA 1960).

One of ordinary skill in the art at the time the invention was made would have been motivated to combine inhibitory von Willebrand factor-specific antibodies in compositions comprising pharmaceutically acceptable carrier in order to test and employ the ability of said inhibitory antibodies to inhibit platelet-mediated or thrombus-mediated interactions and events. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

16. The non-statutory double patenting rejection, whether of the obvious-type or non-obvious-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornam*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman*, 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321 (b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78 (d).

Effective January 1, 1994, a registered attorney or agent of record may sign a Terminal Disclaimer. A Terminal Disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

17. Claims 17-21 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 of U.S. Patent No. 5,916,805 and over claims 1-4 of U.S. Patent No. 6,280,731. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant and patented claims are drawn to the same or nearly the same von Willebrand specific antibodies and compositions thereof.

18. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

19. Claims 17-20 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 3, 5, 13, 15, 18, 20 of U.S. Patent No. 5,916,805 (1449; #AB)

The claims are drawn to same specific von Willebrand monoclonal antibodies produced by the same hybridomas.

If the patented claims 13 and 15, drawn to antithrombotic agents, encompasses compositions rather than compounds drawn to the specific monoclonal antibodies themselves, then instant claims 17-20 would be subject to an obvious double patenting rejection rather than a statutory double patenting rejection with respect to patented claims 13 and 15.

20. No claim is allowed.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 872-9306.

PHILLIP GAMBEL

Phillip Gambel, PhD.
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August 20, 2003